

We claim:

1. Novel gene variants having of SEQ ID Nos. 1 and 2 of Signal Transducer and Activator of Transcription-6 (STAT-6) Gene useful in predicting
5 susceptibility of a subject to atopic disorders, said gene variants having following characteristics:
 - (a) The SEQ ID No.1 has 1- 392 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 125 to 168 of R1 locus, and.
 - 10 (b) the SEQ ID No.2 has 1 to 336 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases of R3 locus.
2. Novel gene variants as claimed in claim 1, wherein SEQ ID No.1 is associated with R1 locus and SEQ ID No.2 is associated with R3 locus of
15 STAT-6 gene.
3. Novel gene variants as claimed in claim 1, wherein a subject is human.
4. Novel gene variants as claimed in claim 1, wherein atopic disorders are selected are from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of
20 STAT-6.
5. Novel gene variants as claimed in claim 4, wherein atopic disorder is asthma.
6. Novel gene variants as claimed in claim 1, wherein said variants are useful are predicting and detecting humans susceptible to atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6.
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7. Novel gene variants as claimed in claim 6, wherein said variants are useful are predicting and detecting humans susceptible to asthma.
8. Novel gene variants as claimed in claim 1, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to
30 atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6.

9. Novel gene variants as claimed in claim 8, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to asthma.
10. Novel gene variants as claimed in claims 1 and 2, wherein said gene variants of locus R1_R3 are associated with specific haplotypes 17_15 and 16_15
11. Novel gene variants as claimed in claim 10, wherein the percentage frequency of R1_R3 locus dinucleotide on haplotypes 17_15 and 16_15 is about 8 % and 20%, respectively in the patients.
12. Novel gene variants as claimed in claim 11, wherein the percentage frequency of R1_R3 locus dinucleotide on allele 17_15 and 16_15 is about 7.1 % and 18.7%, respectively in the patients.
13. Novel gene variants as claimed in claim 1, wherein CA nucleotide repeat is on 17 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.0031 and are associated with asthma.
14. Novel gene variants as claimed in claim 1, wherein CA nucleotide repeat is on 16 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.001 and are associated with asthma.
15. Novel gene variants as claimed in claim 1, wherein haplotypes 17_14 (CA repeat 17 in R1 locus and 14 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001), 23_16 (CA repeat 23 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) and 24_16 (CA repeat 24 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) are associated with protection from asthma.
16. Novel gene variants as claimed in claim 1, wherein the percentage frequency of R1 locus dinucleotide on allele 16 is about 32 % in the patients.
17. Novel gene variants as claimed in claim 16, wherein the percentage frequency of R1 locus dinucleotide on allele is about 30.67 % in the patients.
18. Novel gene variants as claimed in claim 1, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 35 % in the patients.
19. Novel gene variants as claimed in claim 18, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 32 % in the patients.

20. A method of detecting gene variants having SEQ ID Nos. 1 and 2 of STAT-6 for detecting and predicting susceptibility of a subject to atopic disorders said method comprising the steps of:

- 5 (a) isolating DNA or RNA from samples selected from group comprising of whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin or hair,
- (b) designing and synthesizing primers having SEQ ID Nos. 3, 4, 5, 6 and 7
- 10 (c) amplifying the genomic DNA or RNA using primers having SEQ ID Nos. 3, 4, 5, 6 and 7,
- (d) isolating and identifying SEQ ID No.1 using primer combinations having SEQ ID Nos. 3, 4, and 7 and SEQ ID No. 2 using primer combinations having SEQ ID Nos. 5, 6 and 7,
- 15 (e) sequencing the isolated and identified SEQ ID Nos. 1 and 2 of step (d), and
- (f) validating and identifying the specific gene variants having SEQ ID Nos. 1 and 2 computationally by comparing with known STAT-6 gene, wherein the SEQ ID Nos. 1 and 2 has following characteristics
 - 20 (i) the SEQ ID No. has 1- 392 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 125 to 168 bases of R1 locus.
 - (ii) The SEQ ID No. has 1 to 336 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases of R2 locus.
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21. A method as claimed in claim 20, wherein SEQ ID No.1 is associated with R1 locus and SEQ ID No.2 is associated with R3 locus of STAT-6 gene.

30 22. A method as claimed in claim 20, wherein the subject is a human.

23. A method as claimed in claim 20, wherein atopic disorders are selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.

24. A method as claimed in claim 23, wherein atopic disorder selected is asthma.
25. A method as claimed in claim 20, wherein said variants are useful are predicting and detecting humans susceptible to atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
26. A method as claimed in claim 25, wherein said variants are useful are predicting and detecting humans susceptible to asthma.
27. A method as claimed in claim 20, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
28. A method as claimed in claim 27, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to asthma.
29. Novel gene variants as claimed in claims 20 and 21, wherein said gene variants of locus R1_ R3 are associated with specific haplotypes 17_15 and 16_15.
30. A method as claimed in claims 29, wherein the percentage frequency of R1_R3 locus dinucleotide on allele 17_15 and 16_15 is about 8 % and 20%, respectively in the patients.
31. A method as claimed in claim 30, wherein the percentage frequency of R1_R3 locus dinucleotide on haplotypes 17_15 and 16_15 is about 7.1 % and 18.7%, respectively in the patients.
32. A method as claimed in claims 20, wherein CA nucleotide repeat is on 17 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.0031 and are associated with asthma.
33. A method as claimed in claim 20, wherein CA nucleotide repeat is on 16 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.001 and are associated with asthma.
34. A method as claimed in claim 20, wherein haplotypes 17_14 (CA repeat 17 in R1 locus and 14 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001), 23_16 (CA repeat 23 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) and 24_16 (CA repeat 24 in R1

locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) are associated with protection from asthma.

35. A method as claimed in claim 20, wherein the percentage frequency of R1 locus dinucleotide on allele 16 is about 32 % in the patients.

5 36. A method as claimed in claim 35, wherein the percentage frequency of R1 locus dinucleotide on allele is about 30.67 % in the patients.

37. A method as claimed in claim 20, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 35 % in the patients.

10 38. A method as claimed in claim 37, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 32 % in the patients.

39. A method of detecting and predicting predisposition to atopic disorders by screening R1 and R3 locus of STAT-6 gene variants in a subject, said method comprising the steps of:

15 (a) isolating DNA or RNA from samples selected from group comprising of whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin or hair,

(b) designing and synthesizing primers having SEQ ID Nos. 3, 4, 5, 6 and 7

20 (c) amplifying the genomic DNA or RNA using SEQ ID Nos. 3, 4, 5, 6 and 7 by PCR,

(d) isolating and identifying SEQ ID No.1 using primer combinations having SEQ ID Nos. 3, 4, and 7 and SEQ ID No. 2 using primer combinations having SEQ ID Nos. 5, 6 and 7,

25 (e) sequencing the isolated and identified SEQ ID Nos. 1 and 2 of step (d), and

(f) sequencing the amplified PCR product of step (c), and

30 (g) validating and identifying the specific STAT-6 gene variants having SEQ ID Nos. 1 and 2 computationally by comparing with known STAT-6 gene, wherein the SEQ ID Nos. 1 and 2 has following characteristics

(i) the SEQ ID No. has 1- 392 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 125 to 168 bases of locus R1, and

- (ii) the SEQ ID No. has 1 to 336 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases of locus R3.

- 5 40. A method as claimed in claim 39, wherein SEQ ID No.1 is associated with R1 locus and SEQ ID No.2 is associated with R3 locus of STAT-6 gene.
41. A method as claimed in claim 39, wherein the subject is a human.
42. A method as claimed in claim 41, wherein the atopic diseases are selected from group comprising of asthma, atopic dermatitis, autoimmune disorders,
10 inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
43. A method as claimed in claim 42, wherein the atopic disease selected is asthma.
44. A method as claimed in claim 39, wherein said variants are useful are predicting and detecting humans susceptible to atopic disorders selected from
15 group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
45. A method as claimed in claim 44, wherein said variants are useful are predicting and detecting humans susceptible to asthma.
46. A method as claimed in claim 39, wherein said variants are pharmacogenetic
20 markers for predicting and detecting humans susceptible to atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
47. A method as claimed in claim 46, wherein said variants are pharmacogenetic
25 markers for predicting and detecting humans susceptible to asthma.
48. A method as claimed in claims 39 and 40, wherein said gene variants of locus R1_R3 are associated with specific haplotypes 17_15 and 16_15
49. A method as claimed in claim 48, wherein the percentage frequency of R1_R3 locus dinucleotide on haplotypes 17_15 and 16_15 is about 8 % and
30 20%, respectively in the patients.
50. A method as claimed in claim 49, wherein the percentage frequency of R1_R3 locus dinucleotide on haplotypes 17_15 and 16_15 is about 7.1 % and 18.7%, respectively in the patients.

51. A method as claimed in claim 39, wherein CA nucleotide repeat is on 17 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.0031 and are associated with asthma.
52. A method as claimed in claim 39, wherein CA nucleotide repeat is on 16 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.001 and are associated with asthma.
53. A method as claimed in claim 39, wherein haplotypes 17_14 (CA repeat 17 in R1 locus and 14 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001), 23_16 (CA repeat 23 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) and 24_16 (CA repeat 24 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) are associated with protection from asthma.
54. A method as claimed in claim 39, wherein the percentage frequency of R1 locus dinucleotide on allele 16 is about 32 % in the patients.
55. A method as claimed in claim 54, wherein the percentage frequency of R1 locus dinucleotide on allele is about 30.67 % in the patients.
56. A method as claimed in claim 39, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 35 % in the patients.
57. A method as claimed in claim 56, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 32 % in the patients.
58. A method of preparing novel pharmacogenetic markers for detecting and predicting predisposition to atopic disorders of STAT-6 gene in a subject, said method comprising steps of :
- (a) isolating DNA or RNA from samples selected from group comprising of whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin or hair,
 - (b) designing and synthesizing primers having SEQ ID Nos. 3, 4, 5, 6 and 7.
 - (c) amplifying the genomic DNA or RNA using primers having SEQ ID Nos. 3, 4, 5, 6 and 7,
 - (d) isolating and identifying SEQ ID No.1 using primer combinations having SEQ ID Nos. 3, 4, and 7 and SEQ ID No. 2 using primer combinations having SEQ ID Nos. 5, 6 and 7,

- (e) sequencing the isolated and identified SEQ ID Nos. 1 and 2 of step (d), and
- (f) validating and identifying the specific gene variants having SEQ ID Nos. 1 and 2 computationally by comparing with known STAT-6 gene, wherein the SEQ ID Nos. 1 and 2 has following characteristics :
- 5 (i) the SEQ ID No. has 1- 392 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 125 to 168 bases of locus R1, and
- 10 (ii) The SEQ ID No. has 1 to 336 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases of locus R1.
- 15 59. A method gene variants as claimed in claim 58, wherein SEQ ID No.1 is associated with R1 locus and SEQ ID No.2 is associated with R3 locus of STAT-6 gene.
60. A method as claimed in claim 58, wherein the subject is a human.
61. A method as claimed in claim 58, wherein the atopic diseases are selected
- 20 from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
62. A method as claimed in claim 61, wherein the atopic disease selected is asthma.
63. A method as claimed in claim 58, wherein said variants are useful are
- 25 predicting and detecting humans susceptible to atopic disorders selected from group of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
64. A method as claimed in claim 63, wherein said variants are useful are predicting and detecting humans susceptible to asthma.
- 30 65. A method as claimed in claim 58, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune

disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.

66. A method as claimed in claim 65, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to asthma.

5 67. A method as claimed in claims 58 and 59, wherein said gene variants of locus R1_R3 are associated with specific haplotypes 17_15 and 16_15

68. A method as claimed in claim 67, wherein the percentage frequency of R1_R3 locus dinucleotide on haplotypes 17_15 and 16_15 is about 8 % and 20%, respectively in the patients.

10 69. A method as claimed in claim 68, wherein the percentage frequency of R1_R3 locus dinucleotide on haplotypes 17_15 and 16_15 is about 7.1 % and 18.7%, respectively in the patients.

70. A method as claimed in claim 58, wherein CA nucleotide repeat is on 17 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.0031 and are associated with asthma.

71. A method as claimed in claim 58, wherein CA nucleotide repeat is on 16 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.001 and are associated with asthma.

20 72. A method as claimed in claim 58, wherein haplotypes 17_14 (CA repeat 17 in R1 locus and 14 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001), 23_16 (CA repeat 23 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) and 24_16 (CA repeat 24 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) are associated with protection from asthma.

25 73. A method as claimed in claim 58, wherein the percentage frequency of R1 locus dinucleotide on allele 16 is about 32 % in the patients.

74. A method as claimed in claim 73, wherein the percentage frequency of R1 locus dinucleotide on allele is about 30.67 % in the patients.

30 75. A method as claimed in claim 58, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 35 % in the patients.

76. A method as claimed in claim 75, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 32 % in the patients.

77. Pharmacogenetic markers having SEQ ID Nos. 1 and 2 for detecting and predicting predisposition to atopic disorders of STAT-6 gene in a subject said markers comprising of following characteristics:
- (a) the SEQ ID No.1 has 1- 392 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 125 to 168 of R1 locus, and
 - (b) The SEQ ID No.2 has 1 to 336 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases of R3 locus.
78. Pharmacogenetic markers as claimed in claim 77, wherein SEQ ID No.1 is associated with R1 locus and SEQ ID No.2 is associated with R3 locus of STAT-6 gene.
79. Pharmacogenetic markers as claimed in claim 77, wherein a subject is human.
80. Pharmacogenetic markers as claimed in claim 79, wherein atopic disorders are selected are from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
81. Pharmacogenetic markers as claimed in claim 80, wherein atopic disorder is asthma.
82. Pharmacogenetic markers as claimed in claim 77, wherein said variants are useful are predicting and detecting humans susceptible to atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
83. Pharmacogenetic markers as claimed in claim 82, wherein said variants are useful are predicting and detecting humans susceptible to asthma.
84. Pharmacogenetic markers as claimed in claim 77, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.

85. Pharmacogenetic markers as claimed in claim 84, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to asthma.

86. A diagnostic kit for detecting and predicting predisposition to atopic disorders by screening STAT-6 gene variants in a subject, said method comprising the steps of:

(a) isolating DNA or RNA from samples selected from group comprising of whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin or hair,

(b) designing and synthesizing primers having SEQ ID Nos. 3, 4, 5 and 6

(c) amplifying the genomic DNA or RNA using SEQ ID Nos. 3, 4, 5 and 6,

(d) isolating and identifying SEQ ID No.1 using primer combinations having SEQ ID Nos. 3, 4, and 7 and SEQ ID No. 2 using primer combinations having SEQ ID Nos. 5, 6 and 7,

(e) sequencing the isolated and identified SEQ ID Nos. 1 and 2 of step (d), and

(f) sequencing the amplified PCR product of step (c),

(g) validating and identifying the specific STAT-6 gene variants having SEQ ID Nos. 1 and 2 computationally by comparing with known STAT-6 gene, wherein the SEQ ID Nos. 1 and 2 has following characteristics

(i) the SEQ ID No.1 has 1- 392 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 125 to 168 bases, and

(ii) the SEQ ID No.2 has 1 to 336 contiguous nucleotides containing one or more group of GT dinucleotide polymorphisms at positions from 87 to 116 bases.

87. A kit as claimed in claim 86, wherein SEQ ID No.1 is associated with R1 locus and SEQ ID No.2 is associated with R3 locus of STAT-6 gene.

88. A kit as claimed in claim 86, wherein the subject is a human.

89. A kit as claimed in claim 86, wherein the atopic diseases are selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
90. A kit as claimed in claim 89, wherein the atopic disease selected is asthma.
- 5 91. A kit as claimed in claim 86, wherein said variants are useful are predicting and detecting humans susceptible to atopic disorders selected from group of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of STAT-6 gene.
- 10 92. A kit as claimed in claim 91, wherein said variants are useful are predicting and detecting humans susceptible to asthma.
93. A kit as claimed in claim 86, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to atopic disorders selected from group comprising of asthma, atopic dermatitis, autoimmune disorders, inflammatory disorders, fibrosis or other known disorders of
- 15 STAT-6 gene.
94. A kit as claimed in claim 93, wherein said variants are pharmacogenetic markers for predicting and detecting humans susceptible to asthma.
95. A kit as claimed in claims 86 and 87, wherein said gene variants of locus R1_R3 are associated with specific haplotypes 17_15 and 16_15
- 20 96. A kit as claimed in claim 95, wherein the percentage frequency of R1_R3 locus dinucleotide on haplotypes 17_15 and 16_15 is about 8 % and 20%, respectively in the patients.
97. A kit as claimed in claim 96, wherein the percentage frequency of R1_R3 locus dinucleotide on haplotypes 17_15 and 16_15 is about 7.1 % and 18.7%,
- 25 respectively in the patients.
98. A kit as claimed in claim 86, wherein CA nucleotide repeat is on 17 allele of R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.0031 and are associated with asthma.
99. A kit as claimed in claim 86, wherein CA nucleotide repeat is on 16 allele of
- 30 R1 locus and on 15 allele of R3 locus of the STAT- 6 gene having a 'p' value less than 0.001 and are associated with asthma.
100. A kit as claimed in claim 86, wherein haplotypes 17_14 (CA repeat 17 in R1 locus and 14 in R3 locus of the STAT- 6 gene having a 'p' value less

than 0.00001), 23_16 (CA repeat 23 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) and 24_16 (CA repeat 24 in R1 locus and 16 in R3 locus of the STAT- 6 gene having a 'p' value less than 0.00001) are associated with protection from asthma.

- 5 101. A kit as claimed in claim 86, wherein the percentage frequency of R1 locus dinucleotide on allele 16 is about 32 % in the patients.
102. A kit as claimed in claim 101, wherein the percentage frequency of R1 locus dinucleotide on allele is about 30.67 % in the patients.
103. A kit as claimed in claim 86, wherein the percentage frequency of R3
10 locus dinucleotide on allele 15 is about 35 % in the patients.
104. A kit as claimed in claim 103, wherein the percentage frequency of R3 locus dinucleotide on allele 15 is about 32 % in the patients.